Outcomes of carotid endarterectomy under general and regional anesthesia from the American College of Surgeons' National Surgical Quality Improvement Program

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Objective: **Despite multiple studies over more than 3 decades, there still is no consensus about the influence of anesthesia type on postoperative outcomes following carotid endarterectomy (CEA). The objective of this study was to investigate whether anesthesia type, either general anesthesia (GA) or regional anesthesia (RA), independently contributes to the risk of postoperative cardiovascular complications or death using the American College of Surgeons' National Surgical Quality Improvement Program (ACS NSQIP) database.**

Methods: **Retrospective analysis of elective cases of CEA from 2005 through 2009 was performed. A propensity score model using 45 covariates, including demographic factors, comorbidities, stroke history, measures of general health, and laboratory values, was used to adjust for bias and to determine the independent influence of anesthesia type on postoperative stroke, myocardial infarction (MI), and death.**

Results: **Of 26,070 cases listed in the ACS NSQIP database, GA and RA were used in 22,054 (84.6%) and 4016 (15.4%) cases, respectively. Postoperative stroke, MI, and death occurred in 360 (1.63%), 133 (0.6%), and 154 (0.70%) patients of the GA group, respectively, and in 58 (1.44%), 11 (0.27%), and 27 (0.67%) patients of the RA group, respectively. Stratification by propensity score quintile and adjustment for covariates demonstrated GA to be a significant risk factor for postoperative MI with an adjusted odds ratio (OR) and confidence interval (CI) of 2.18 (95% CI, 1.17-4.04), $P = .01$ in the entire study population. The OR for MI was 5.41 (95% CI, 1.32-22.16; $P = .019$) in the subgroup of patients with preoperative neurologic symptoms, and 1.44 (95% CI, 0.71-2.90; $P = .31$) in the subgroup of patients without preoperative neurologic symptoms.**

Conclusions: **This analysis of a large, prospectively collected and validated multicenter database indicates that GA for CEA is an independent risk factor for postoperative MI, particularly in patients with preoperative neurologic symptoms. (J Vasc Surg 2012;56:81-8.)**

In the 1990s, the North American Symptomatic Carotid Endarterectomy Trial (NASCET)[1] and the European Carotid Surgery Trial (ECST)[2] established carotid endarterectomy (CEA) as the gold standard for the treatment of symptomatic moderate to high-grade carotid artery stenosis. In selected patients, superior outcomes of surgical intervention as compared to medical treatment for high-grade asymptomatic carotid artery stenosis followed,[3,4] but the clear benefit of surgery demonstrated at that time has since then been challenged by refinement of nonoperative care for carotid artery stenosis. Better medication, most notably statins,[5] and stronger antiplatelet agents, as well as endovascular techniques such as carotid artery stenting, have been proposed as alternatives to open surgery.

Numerous studies have confirmed the safety of CEA but have also identified risk factors for perioperative complications, particularly stroke, myocardial infarction (MI), and nerve injury.[6-8] CEA is most commonly performed under general anesthesia (GA); alternatively, regional anesthesia (RA) using a cervical plexus block may be employed. The influence of anesthesia type on postoperative outcomes has been a controversial topic, and studies have been contradictory. While some studies suggested better outcomes with RA,[9-11] other studies found no significant differences between GA and RA.[12,13] The largest multicenter, randomized controlled trial to date, GALA (General Anesthesia versus Local Anesthesia for carotid surgery), also did not demonstrate a statistically significant difference between GA and RA with regard to postoperative stroke, MI, or death within 30 days after surgery.[13]

The objective of this study was to determine the independent contribution of the anesthesia type used during CEA to the postoperative occurrence of stroke, MI, and death, by examining the largest cohort of carotid endarterectomies studied to date in the rigorously maintained, prospectively collected database of the American College of

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Surgeons' National Surgical Quality Improvement Program (ACS NSQIP).

METHODS

This study was approved by the Institutional Review Board at Saint Joseph Mercy Health System. Retrospective analysis of CEA cases from 2005 through 2009 in the ACS NSQIP database was performed. This quality improvement program originated in the Veterans Affairs system almost 2 decades ago, and the ACS NSQIP database is maintained by the American College of Surgeons. Over 100 precisely defined variables are collected on surgical patients, including demographic characteristics, comorbidities, laboratory values, intraoperative events, and 30-day postoperative outcomes. During the study period, more than 200 participating hospitals nationwide systematically collected these data prospectively. Data abstractors ("clinical nurse reviewers") at each participating hospital are subjected to initial certification, continuous training, examination, and audits. The high quality and validity of the ACS NSQIP database has been demonstrated in several reports and studies,[14-17] and inter-rater reliability audits have demonstrated a disagreement rate on variables in 2008 of <2%.[18]

Study population. Included in this study were all cases of elective CEA, as defined by the Common Procedural Terminology (CPT) code 35301. Cases were stratified into the GA group, if the anesthesia type listed in the ACS NSQIP database was "general anesthesia"; or into the RA group, if the type of anesthesia listed was "regional," "local," or "monitored anesthesia care." Additionally, two subgroups were defined for patients with and without preoperative neurologic symptoms. Patients were classified as having symptomatic disease if one or more of the following comorbidities were recorded in the ACS NSQIP database: (1) history of stroke with persistent neurologic deficit; (2) history of stroke without persistent neurologic deficit; or (3) history of transient ischemic attack (TIA). All other patients were considered to have asymptomatic carotid artery disease. Case exclusion criteria were age under 18 years, emergent procedures, patients designated American Society of Anesthesiologists (ASA) classes 5 and 6, mechanically ventilated patients, comatose patients, the presence of a central nervous system tumor, the presence of ascites, and an anesthesia type listed as "epidural," "spinal," "none," "other," or "unknown," which was considered to be a potentially erroneous entry.

Primary outcomes of interest were postoperative stroke, MI, and death occurring within 30 days of operation. Per ACS NSQIP guidelines, a postoperative stroke was defined by the development of an embolic, thrombotic, or hemorrhagic vascular accident with motor, sensory, or cognitive dysfunction persisting for more than 24 hours. Postoperative MI was documented in the database if the clinical nurse reviewer found any one of the following criteria in a patient's medical record: (1) electrocardiogram changes indicative of MI (ST segment elevation >1 mm in two or more contiguous leads, new left bundle branch block, or a new Q-wave in two or more contiguous leads); (2) new elevation of troponin levels greater than three times the reference range in the setting of suspected myocardial ischemia; or (3) a physician's documented diagnosis of MI.

Secondary outcomes were cardiac arrest requiring cardiopulmonary resuscitation and length of hospital stay until discharge. Additional risk factors for postoperative stroke, MI, and death were determined in a multivariable logistic regression model, after stratifying on propensity score quintile and controlling for significant covariates.

Statistical analysis. Initial comparisons of baseline demographic and clinical characteristics for the GA and RA groups were made using Pearson χ^2 tests for categorical variables and independent sample *t*-tests for continuous variables. Initial unadjusted estimates of the incidence of postoperative stroke, MI, and death in the GA and RA group were calculated. A multivariable logistic regression analysis was performed to predict each postoperative outcome after stratifying on propensity score quintile and including any other covariates that had been found to be significant predictors of each outcome in an initial simple logistic regression model.

Because this was not a randomized controlled trial, it was expected that patients in the GA group and the RA group would differ in some clinical characteristics. To aid in making an unbiased comparison between patient groups, and to adjust for the potential differences between patients in these two anesthesia groups, a propensity score analysis was used.[19] To implement the propensity score method, the probability of receiving GA was estimated for each patient using a multivariate logistic regression model, based on a list of covariates likely to be related to the choice of anesthesia type. These covariates included 45 baseline characteristics: demographic factors, comorbidities, stroke history, measures of general health, and laboratory values.

Missing data were found for some laboratory values. To allow for the inclusion of these cases, each test result was classified as normal, abnormal, or missing, in which case a dummy variable was included in the propensity score model. The propensity score model also included interaction terms, where appropriate, to improve the model fit. To ensure that the propensity score method had produced comparable groups, the balance for covariates between the two anesthesia groups was assessed after propensity score adjustment by using a logistic regression stratified on propensity score quintile for categorical predictors and an analysis of variance model controlling for propensity score quintile for continuous predictors.

The relationship of anesthesia type to stroke, MI, and death was then estimated in the entire study population and in the two subgroups of asymptomatic and symptomatic patients, using a logistic regression analysis for each outcome, stratified on propensity score quintile, as reported by Rubin.[19] The Breslow-Day test[20] for homogeneity of odds ratios (ORs) was used to ascertain whether the stratified ORs for anesthesia type were consistent across propensity score quintiles. A nonsignificant Breslow-Day test would provide evidence that the relationship between anesthesia

Table I. Case details and selected variables in the GA group and the RA group before and after stratification on propensity score[a]

	Anesthetic method		P *value for comparison*	
Risk factors	*GA No. (%) 22,054 (84.6)*	*RA No. (%) 4016 (15.4)*	*Before propensity score adjustment*	*After propensity score adjustment*
Demographics				
Age (mean, SD)	70.9 (9.6)	72.0 (9.4)	<.01[b]	.80
Female	9150 (41.5)	1587 (39.5)	.02[b]	.87
African American	570 (2.6)	70 (1.7)	<.01[b]	.82
Body mass index >25 kg/m^2	8457 (38.4)	1600 (39.8)	.03[b]	.84
General factors				
Tobacco use	6288 (28.5)	1007 (25.1)	<.01[b]	.89
ASA class				
1: Healthy	41 (0.2)	3 (0.1)	.25	.57
2: Mild systemic disease	2051 (9.3)	423 (10.5)	<.01[b]	.51
3: Severe systemic disease	17,078 (77.4)	3166 (78.8)	<.01[b]	.84
4: Severe systemic disease (life-threatening)	2886 (13.1)	424 (10.6)	Ref	Ref
Functional status				
Partially dependent	1092 (5.0)	195 (4.9)	.03[b]	.89
Totally dependent	98 (0.4)	8 (0.2)	.77	.38
Neurovascular comorbidities				
History of TIA	6123 (27.8)	1100 (27.4)	.63	.90
History of stroke (persistent deficit)	3379 (15.3)	512 (12.8)	<.01[b]	.82
History of stroke (without persistent deficit)	2033 (9.22)	358 (8.9)	.54	.95
Hemiplegia	1304 (5.9)	163 (4.1)	<.01[b]	.70
Impaired sensorium	143 (0.7)	24 (0.6)	.71	.99
History of peripheral vascular disease	2114 (9.6)	354 (8.8)	.12	.94
History of peripheral vascular disease (with pain at rest)	202 (0.9)	47 (1.2)	.13	.87
Cardiac comorbidities				
Antihypertensive medication	18,777 (85.1)	3460 (86.2)	.10	.93
History of congestive heart failure (within 30 days)	216 (1.0)	35 (0.9)	.52	.83
History of angina (within 30 days)	601 (2.7)	87 (2.2)	.04[b]	.86
History of MI (within 6 months)	349 (1.6)	48 (1.2)	.07	.82
History of percutaneous coronary intervention	4084 (18.5)	750 (18.7)	.81	.98
History of cardiac surgery	5103 (23.1)	918 (22.9)	.70	.94
Abnormal laboratory values				
White blood cells	885 (4.0)	154 (3.8)	.29	.97
Hematocrit	7471 (33.9)	1289 (32.1)	.47	.83
Platelet count	1544 (7.0)	280 (7.0)	.93	.95
Creatinine	5761 (26.1)	1045 (26.0)	.81	.96
International normalized ratio	521 (2.4)	110 (2.7)	.05[b]	.52

ASA, American Society of Anesthesiologists; *GA,* general anesthesia; *MI,* myocardial infarction; *RA,* regional anesthesia; *Ref,* reference category (for comparison with each covariate); *SD,* standard deviation; *TIA,* transient ischemic attack.

[a]The complete table, including all variables used in the propensity score model can be accessed online.

[b]Denotes $P < .05$.

type and outcome of interest did not differ significantly between patients with varying propensities to undergo CEA under GA or RA. Statistical significance for all analyses was indicated by $P < .05$. Analyses were performed using SAS software for Windows, release 9.2 (SAS Inc, Cary, NC).

RESULTS

The ACS NSQIP database listed 26,950 carotid endarterectomies (CPT code 35301) between 2005 and 2009, with 26,070 cases meeting inclusion criteria. GA was used in 22,054 (84.6%) cases, while RA was used in 4016 (15.4%) cases. Of the entire group, 56.4% (n = 14,716) were asymptomatic, while 43.6% (n = 11,354) were symptomatic. A comparison of selected demographic characteristics, comorbidities, and other clinical variables for the GA group and the RA group before and after adjusting for propensity score quintile is shown in Table I (the complete Table I, including all variables used for the propensity score model, is available online only). Twenty of the 45 covariates differed significantly ($P < .05$) between the two groups prior to stratification

Table II. Unadjusted and adjusted ORs for stroke, MI, and death after CEA under GA versus RA for the entire study population

	Before propensity score adjustment			*After propensity score adjustment*		
Outcome	*OR*	*95% CI*	P *value*	*OR*	*95% CI*	P *value*
Stroke	1.13	0.86-1.49	.38	1.06	0.79-1.39	.71
MI	2.21	1.19-4.09	.01[a]	2.18	1.17-4.04	.01[a]
Death	1.04	0.69-1.57	.86	0.99	0.65-1.49	.95

CEA, Carotid endarterectomy; *CI,* confidence interval; *GA,* general anesthesia; *MI,* myocardial infarction; *OR,* odds ratio; *RA,* regional anesthesia.
[a]Denotes statistical significance with $P < .05$.

Table III. Unadjusted and adjusted ORs for stroke, MI, and death after CEA in patients without a preoperative history of neurologic symptoms

	Before propensity score adjustment			*After propensity score adjustment*		
Outcome	*OR*	*95% CI*	P *value*	*OR*	*95% CI*	P *value*
Stroke	1.09	0.71-1.69	.70	1.07	0.69-1.67	.75
MI	1.39	0.69-2.79	.36	1.44	0.71-2.90	.31
Death	0.96	0.53-1.75	.89	0.93	0.51-1.70	.82

CEA, Carotid endarterectomy; *CI,* confidence interval; *MI,* myocardial infarction; *OR,* odds ratio.

by propensity score. After stratification, no significant difference was found between the GA group and the RA group for any of these variables, indicating that the propensity score method had eliminated the initial differences between the two groups and provided marginal balance on these measured covariates.

The Breslow-Day test for homogeneity of ORs was nonsignificant for each outcome (stroke, $P = .46$; MI, $P = .49$; death, $P = .22$), indicating that the ORs calculated were similar across the five propensity score strata, regardless of the probability of a patient to undergo CEA under GA or RA.

Postoperative stroke, MI, and death occurred in 360 (1.63%), 133 (0.6%), and 154 (0.70%) patients in the GA group, respectively. Postoperative stroke, MI, and death occurred in 58 (1.44%), 11 (0.27%), and 27 (0.67%) patients in the RA group, respectively. Unadjusted and propensity-score adjusted OR and 95% confidence intervals (CI) for stroke, MI, and death in the entire study population demonstrated a significantly increased risk for MI with GA and are shown in Table II. Additional predictors for postoperative MI determined by multivariable logistic regression were age and a history of angina within 30 days prior to the operation (OR, 1.04; 95% CI, 1.02 to 1.06; $P < .001$, and OR, 2.83; 95% CI, 1.52 to 5.25; $P = .001$, respectively).

Postoperative stroke, MI, and death in 12,343 asymptomatic patients who underwent CEA under GA occurred in 136 (1.10%), 65 (0.53%), and 65 (0.53%) cases, respectively. In 2373 asymptomatic patients who underwent CEA under RA, postoperative stroke, MI, and death occurred in 24 (1.01%), nine (0.38%), and 13 (0.55%) patients, respectively. Unadjusted and propensity-score adjusted OR and 95% CI for stroke, MI, and death in asymptomatic patients did not demonstrate any significant associations and are shown in Table III. Multivariable logistic regression analysis determined age and a history of angina within 30 days prior to the operation to be significant predictors for postoperative MI (OR, 1.06; 95% CI, 1.02 to 1.09; $P = .001$, and OR, 3.79; 95% CI, 1.61 to 8.91; $P = .002$, respectively).

Postoperative stroke, MI, and death in 9711 symptomatic patients who underwent CEA under GA occurred in 224 (2.31%), 68 (0.70%), and 89 (0.92%) cases, respectively. In 1643 symptomatic patients who underwent CEA under RA, postoperative stroke, MI, and death occurred in 34 (2.07%), two (0.12%), and 13 (0.79%) patients, respectively. Unadjusted and propensity-score adjusted OR and 95% CI for stroke, MI, and death in symptomatic patients demonstrated a significantly increased risk for MI with GA and are shown in Table IV. A significant risk factor for postoperative MI determined by multivariable logistic regression was an abnormal hematocrit level (OR, 1.70; 95% CI, 1.01 to 2.87; $P = .05$).

Additional significant risk factors for stroke and death in symptomatic and asymptomatic patients and in the entire study population are shown in Table V (online only).

Postoperative cardiac arrest occurred in 73 (0.28%) cases. It occurred in 0.30% of patients in the GA group (n = 67) and in 0.15% of patients in the RA group (n = 6). This trend did not quite reach statistical significance ($P = .08$).

The difference in the length of hospital stay (LOS; mean ± SD) was highly significant between the GA group with 2.08 ±3.60 days and the RA group with 1.68 ±2.81 days ($P = .0001$). LOS increased to 7.29 (±8.08) days and 6.45 (±10.24) days in the GA and RA groups, respectively, in patients with postoperative MI.

Table IV. Unadjusted and adjusted ORs for stroke, MI, and death after CEA in patients with a preoperative history of neurologic symptoms

	Before propensity score adjustment			*After propensity score adjustment*		
Outcome	*OR*	*95% CI*	P *value*	*OR*	*95% CI*	P *value*
Stroke	1.12	0.78-1.61	.55	1.03	0.71-1.48	.89
MI	5.78	1.42-23.61	.01[a]	5.41	1.32-22.16	.019[a]
Death	1.08	0.61-1.90	.80	1.04	0.59-1.85	.89

CEA, Carotid endarterectomy; *CI,* confidence interval; *MI,* myocardial infarction; *OR,* odds ratio.
[a]Denotes statistical significance with $P < .05$.

DISCUSSION

In this analysis of the large, multicenter ACS NSQIP database, GA was found to be an independent risk factor for MI after CEA. The odds for this complication were particularly high in the subgroup of patients with preoperative neurologic symptoms. Anesthesia type did not influence the incidence of postoperative stroke or death. The overall rate of stroke, MI, and death after CEA in both symptomatic and asymptomatic patients was extremely low. These findings are similar to those in a previous ACS NSQIP analysis of only asymptomatic patients.[8]

A retrospective review suggesting that RA with periprocedural neurologic monitoring results in fewer cardiopulmonary complications and may be safer than GA was published as early as 1982.[21] After the dramatic increase in the volume of CEAs following NASCET[1] and ECST,[2] several subsequent studies demonstrated varying results regarding the type of anesthesia used and cardiovascular complications. Watts et al[22] performed a retrospective review of 548 cases of CEA and reported a significantly higher rate of MI with GA (8.4%) than with RA (2.3%). The authors suggested that higher rates of hemodynamic variability in patients undergoing CEA under GA could be responsible for this finding. Allen et al[11] reviewed 584 cases of CEA performed for predominantly symptomatic patients and found fewer postoperative cardiac complications with the use of RA. They did not report any significant difference in the occurrence of postoperative stroke and death. In addition, they found RA to be more resource-efficient, leading to fewer intraoperative shunt insertions and shorter postoperative LOS.[11] In our study, patients in the GA group also had a significantly longer LOS than patients in the RA group. Considering the small absolute difference (2.08 vs 1.68 days), this statistically significant difference may not represent a clinically significant difference.

Similar findings with regard to anesthesia type were reported by McCarthy et al,[23] who prospectively analyzed 240 patients undergoing CEA under GA and RA. No significant difference between GA and RA was found in regard to perioperative stroke and mortality. Postoperative MI was not among the outcomes studied. RA was shown to result in fewer episodes of intraoperative hypotension, which may be beneficial for patients at risk for myocardial ischemia. In addition to a significantly lower rate of intraoperative shunting and improved hemodynamic stability, this study also demonstrated a decreased LOS and better cost-effectiveness, results similar to other studies.[24,25]

The benefits of RA for CEA suggested in multiple retrospective analyses and cohort studies were not confirmed in the largest prospective clinical trial to date (GALA). This multinational, multicenter trial randomized 3526 patients with symptomatic and asymptomatic carotid disease to CEA under either GA or RA and examined a primary composite outcome of stroke, MI, and death within 30 days of CEA. The study population was similar to patients included in the ACS NSQIP with regard to several demographic characteristics and comorbidities, but GALA included substantially more tobacco users (80% vs 27%) and fewer asymptomatic patients (39% vs 56%). More patients in GALA were classified as ASA classes 1 and 2 (65% vs 10%), whereas almost 90% of patients in the ACS NSQIP database belonged to ASA classes 3 and 4. A statistically significant difference between GA and RA with regard to the occurrence of the composite outcome, or the occurrence of either stroke, MI, or death individually, was not demonstrated in GALA. This was true for symptomatic and asymptomatic patients.[13]

Even though results from the GALA trial suggest that GA and RA are equivalent with regard to postoperative complications, there were several interesting observations and trends that differed between anesthesia type. In patients with contralateral carotid artery occlusion, the composite outcome occurred twice as often in patients under GA than RA, with an OR of 0.47 (0.20 to 1.15), a trend that failed to reach statistical significance ($P = .098$). With regard to hemodynamic stability, there was a significant difference between anesthesia types, with patients in the GA group requiring vasopressor support more often than patients in the RA group ($P < .001$). Hemodynamic stability might have contributed to the trend seen in our results that demonstrated fewer intra- and postoperative cardiac arrests in the RA group than in the GA group, which did not quite reach statistical significance. Finally, a cost-effectiveness analysis of the GALA trial[25] demonstrated a slight economic advantage of RA over GA, mostly a result of less intraoperative device use (shunts) and shorter time in the intensive care unit.

In the current study, anesthesia type did not influence the incidence of intra- and postoperative cerebrovascular accidents, which is in accordance with most existing stud-

ies.[26] Nevertheless, several authors consider RA to be safer from a neurologic perspective, because it allows for continuous monitoring of cognitive function and early detection of cerebral hypoperfusion. In addition, patients undergoing CEA under RA generally require fewer shunt insertions, thus avoiding associated thromboembolic complications. These patients may also have improved cerebral circulation[27] and autoregulation.[28] Short-term stroke rates after CEA have been reported to be as low as 1%[8] or more than 5%,[7,11] with the extremes reflecting low-risk, asymptomatic and high-risk, symptomatic patients, respectively. Major risk factors for postoperative stroke include symptomatic carotid artery stenosis and various systemic factors, including advanced age, cardiac disease, diabetes, and limited functional status.[6,7] These findings suggest that clinical status and comorbidities, both of which were adjusted for in the propensity model, might be more important determinants of perioperative stroke rate associated with CEA than anesthesia type. Given the severe implications of cerebrovascular accidents on patients' quality of life, minimizing the risk of perioperative stroke is arguably of highest priority.

The higher incidence of perioperative cardiac complications under GA may be explained by the complex pathophysiologic processes of myocardial ischemia, which are the consequence of a mismatch between increased oxygen demand (in the operative setting frequently caused by catecholamine release, tachycardia, or the use of vasoactive medication) and decreased oxygen supply. The latter factor can be influenced by the hemodynamic effects of GA; postinduction hypotension is a common effect of general anesthetics,[29] and lower mean arterial pressures with GA than with RA were demonstrated in both clinical trials[27] and database analyses.[23,30] GA can negatively affect the balance between sympathetic and parasympathetic tone, and GA has been found to cause a greater degree of hemodynamic instability, leading to more variation in systolic blood pressure and heart rate during the intra- and postoperative phase, subsequently increasing the demand for vasoactive medication.[10,30,31] GA might also have a more profound influence on the coagulation system, thus increasing the risk for thromboembolic events.[32,33]

While anesthesia type only influenced the occurrence of postoperative MI, this study identified several patient-related risk factors that were significantly associated with an increased risk for postoperative stroke, MI, or death. In general, older patients with severe comorbidities, such as chronic obstructive pulmonary disease or peripheral vascular disease, were at higher risk for postoperative death, while more specific cardiac (eg, angina within 30 days prior to the operation) and neurologic (eg, history of stroke or TIA) comorbidities increased the risk for postoperative MI and stroke, respectively. Similar associations were also demonstrated in two recent ACS NSQIP analyses focusing on the identification of preoperative risk factors for postoperative complications.[8,34] The risk factors identified in these studies were not identical to those determined in this analysis and also differed among each other. This may be explained by the smaller dataset used in these studies, different primary outcomes, and/or by variations in the statistical models.

The strength of this study is that it is derived from a large, rigorously maintained, and prospectively collected database from more than 200 hospitals in the U.S. The highly trained and certified ACS NSQIP clinical nurse reviewers are experienced in abstracting these clinical variables and provide high-quality data.[15,17,18] With over 26,000 cases, this is the largest cohort of CEA cases studied to date. The large study population in our database is particularly important when evaluating outcomes that are severe but infrequent, such as stroke and death after CEA, the evaluation of which is difficult to achieve in a randomized controlled trial. Participating institutions nationwide range from small community hospitals to large academic centers, and the study population therefore reflects a spectrum of demographics and comorbidities encountered in everyday clinical practice, compared with the often highly selective patient population studied in randomized controlled trials. Additionally, database analyses avoid the ethical and financial problems frequently encountered in clinical trials.

Using logistic regression and stratification on propensity score allowed us to reduce the bias inherent to databases and to determine the independent contribution of anesthesia type to postoperative complications. The propensity score method was successful in removing differences between the groups on all chosen variables. The effectiveness of propensity score models to adjust for the differences between several study groups has been demonstrated previously.[35-38]

However, the analysis of a surgical database that lacks specific vascular data has several limitations. No information was available regarding specific preoperative assessment for vascular disease and cardiac testing. The precise degree of carotid artery stenosis and the presence of contralateral carotid artery stenosis were not known. The ACS NSQIP database did not record data on the utilization of antiplatelet agents or perioperative β-blockers. Specifics about the anesthesia types used (beyond GA or RA) and operative details, such as the use of intraoperative shunting, were not available. Additionally, patients in the ACS NSQIP database were not subjected to increased postoperative surveillance or additional testing, and therefore more specific information about postoperative stroke and MI such as severity of symptoms was not available. Finally, as propensity score stratification for patient matching does not represent true randomization, it can only adjust for known and measured confounders, and missing information in the database, particularly among laboratory values, required the introduction of dummy variables in the statistical model.

CONCLUSIONS

GA is associated with an increased risk for MI after CEA, particularly in the subgroup of patients with preoperative neurologic symptoms. In eligible patients and at

institutions experienced in this technique, regional anesthesia should be considered the anesthetic type of choice.

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AUTHOR CONTRIBUTIONS

Conception and design: SW, NM, KW, RL, WW, MH
Analysis and interpretation: SW, KW, WW, MH
Data collection: SW, KW, RL
Writing the article: SW, NM, KW, RL, WW, MH
Critical revision of the article: SW, NM, KW, RL, WW, MH
Final approval of the article: SW, NM, KW, RL, WW, MH
Statistical analysis: SW, KW
Obtained funding: RL
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Table I (online only). Case details and variables in the GA group and the RA group before and after stratification on propensity score

	Anesthetic method		P *value for comparison*	
Risk factors	*GA No. (%) 22,054 (84.6)*	*RA No. (%) 4016 (15.4)*	*Before propensity score adjustment*	*After propensity score adjustment*
Demographics				
Age (mean, SD)	70.9 (9.6)	72.0 (9.4)	<.01[a]	.80
Female	9150 (41.5)	1587 (39.5)	.02[a]	.87
Race				
White	12,210 (55.4)	2148 (53.5)	Ref	Ref
African American	570 (2.6)	70 (1.7)	<.01[a]	.82
Missing	9274 (42.1)	1798 (44.8)	<.01[a]	.96
Body mass index category				
Underweight	401 (1.8)	69 (1.7)	.95	.96
Normal	5839 (26.5)	1093 (27.2)	.09	.96
Overweight	8457 (38.4)	1600 (39.8)	.03[a]	.84
Obese	7021 (31.8)	1217 (30.3)	Ref	Ref
Missing	336 (1.5)	37 (0.9)	<.01[a]	.46
General factors				
Tobacco use	6288 (28.5)	1007 (25.1)	<.01[a]	.89
Alcohol abuse	978 (4.4)	161 (4.1)	.23	.97
ASA class				
1: Healthy	41 (0.2)	3 (0.1)	.25	.57
2: Mild systemic disease	2051 (9.3)	423 (10.5)	<.01[a]	.51
3: Severe systemic disease	17,078 (77.4)	3166 (78.8)	<.01[a]	.84
4: Severe systemic disease (life-threatening)	2886 (13.1)	424 (10.6)	Ref	Ref
Functional status				
Independent	20,864 (94.6)	3813 (95.0)	Ref	Ref
Partially dependent	1092 (5.0)	195 (4.9)	.03[a]	.89
Totally dependent	98 (0.4)	8 (0.2)	.77	.38
Prior operation (within 30 days)				
No	20,022 (90.8)	3716 (1.4)	Ref	Ref
Yes	252 (1.1)	57 (1.4)	.18	.94
Missing	1780 (0.1)	243 (6.1)	<.01[a]	.89
Sepsis/SIRS	176 (0.8)	26 (0.7)	.32	.90
Neurovascular comorbidities				
History of TIA	6123 (27.8)	1100 (27.4)	.63	.90
History of stroke (persistent deficit)	3379 (15.3)	512 (12.8)	<.01[a]	.82
History of stroke (without persistent deficit)	2033 (9.22)	358 (8.9)	.54	.95
Hemiplegia	1304 (5.9)	163 (4.1)	<.01[a]	.70
Impaired sensorium	143 (0.7)	24 (0.6)	.71	.99
History of peripheral vascular disease	2114 (9.6)	354 (8.8)	.12	.94
History of peripheral vascular disease (with pain at rest)	202 (0.9)	47 (1.2)	.13	.87
Cardiac comorbidities				
Antihypertensive medication	18,777 (85.1)	3460 (86.2)	.10	.93
History of congestive heart failure (within 30 days)	216 (1.0)	35 (0.9)	.52	.83
History of angina (within 30 days)	601 (2.7)	87 (2.2)	.04[a]	.86
History of MI (within 6 months)	349 (1.6)	48 (1.2)	.07	.82
History of percutaneous coronary intervention	4084 (18.5)	750 (18.7)	.81	.98
History of cardiac surgery	5103 (23.1)	918 (22.9)	.70	.94
Pulmonary comorbidities				
Current pneumonia	33 (0.2)	4 (0.1)	.44	.93
Dyspnea				
None	17,773 (80.6)	3285 (81.8)	Ref	Ref
At rest	271 (1.2)	47 (1.2)	.69	.99
With moderate exertion	4010 (18.2)	684 (17.0)	.08	.99

ASA, American Society of Anesthesiologists; *GA,* general anesthesia; *MI,* myocardial infarction; *RA,* regional anesthesia; *Ref,* reference category (for comparison with each covariate); *SD,* standard deviation; *SIRS,* systemic inflammatory response syndrome; *TIA,* transient ischemic attack.
[a]$P < .05$.

Table I (online only). Continued

Risk factors	*Anesthetic method*		P *value for comparison*	
	GA No. (%) 22,054 (84.6)	*RA No. (%) 4016 (15.4)*	*Before propensity score adjustment*	*After propensity score adjustment*
History of severe chronic obstructive pulmonary disease	2271 (10.3)	399 (9.9)	.49	.97
Chemotherapy (within 30 days)	49 (0.2)	14 (0.4)	.14	.70
Disseminated cancer	52 (0.2)	8 (0.2)	.66	.98
Weight loss >10% (within 6 months)	130 (0.6)	25 (0.6)	.80	.83
Renal comorbidities				
Hemodialysis	221 (1.0)	33 (0.8)	.29	.99
Endocrine/other comorbidities				
Diabetes	6091 (27.6)	1083 (27.0)	.40	.95
Steroids	460 (2.1)	86 (2.1)	.82	.93
Bleeding disorder	4481 (20.3)	815 (20.3)	.97	.96
White blood cells				
No	18,570 (84.2)	3394 (84.5)	Ref	Ref
Yes	885 (4.0)	154 (3.8)	.29	.97
Missing	2599 (11.8)	469 (11.7)	.78	.98
Hematocrit				
No	11,454 (51.9)	2215 (52.9)	Ref	Ref
Yes	7471 (33.9)	1289 (32.1)	.47	.83
Missing	3129 (14.2)	602 (15.0)	.06	.96
Platelet count				
No	18,681 (84.7)	3407 (84.8)	Ref	Ref
Yes	1544 (7.0)	280 (7.0)	.93	.95
Missing	1829 (8.29)	329 (8.2)	.83	.97
Blood urea nitrogen				
No	19,796 (88.8)	3473 (86.5)	Ref	Ref
Yes	803 (3.6)	161 (4.0)	.13	.79
Missing	1455 (6.6)	382 (9.5)	<.01[a]	.15
Creatinine				
No	15,302 (69.4)	2750 (68.5)	Ref	Ref
Yes	5761 (26.1)	1045 (26.0)	.81	.96
Missing	991 (4.5)	221 (5.5)	<.01[a]	.88
Prothrombin time				
No	12,613 (57.2)	2094 (52.1)	Ref	Ref
Yes	2076 (9.4)	344 (8.6)	<.01[a]	.67
Missing	7365 (33.4)	1578 (39.3)	<.01[a]	.55
International normalized ratio				
No	15,449 (70.0)	2639 (65.7)	Ref	Ref
Yes	521 (2.4)	110 (2.7)	.05[a]	.52
Missing	6084 (27.6)	1267 (31.6)	<.01[a]	.79
Partial thromboplastin time				
No	12,613 (57.2)	2094 (52.1)	Ref	Ref
Yes	2076 (9.4)	344 (8.6)	.98	.98
Missing	7365 (33.4)	1578 (39.3)	<.01[a]	.60
Aspartate amino transferase				
No	10,092 (45.8)	1693 (42.2)	Ref	Ref
Yes	727 (3.3)	110 (2.7)	.33	.99
Missing	11,235 (50.9)	2213 (55.1)	<.01[a]	.71
Albumin				
No	9787 (44.4)	1600 (39.8)	Ref	Ref
Yes	697 (3.2)	123 (3.1)	.45	.99
Missing	11,570 (52.5)	2293 (57.1)	<.01[a]	.88
Alkaline phosphatase				
No	9802 (44.5)	1547 (38.5)	Ref	Ref
Yes	650 (3.0)	103 (2.6)	.97	.97
Missing	11,602 (52.6)	2366 (58.9)	<.01[a]	.53
Bilirubin				
No	9580 (43.4)	1515 (37.7)	Ref	Ref
Yes	793 (3.6)	126 (3.1)	.96	.97
Missing	11,681 (53.0)	2375 (59.1)	<.01[a]	.56

Table V (online only). Significant risk factors for stroke and death after carotid endarterectomy in the entire study population and in patients with and without a preoperative history of neurologic symptoms

Outcome	*Preoperative risk factor*	P *value*
Stroke (all patients)	Angina (within 30 days prior to operation)	.03
	Hemiplegia	<.01
	Stroke without persistent neurologic deficit	<.01
	Stroke with persistent neurologic deficit	<.0001
	Transient ischemic attack	<.001
Stroke (symptomatic patients)	Hemiplegia	.01
	Stroke without persistent neurologic deficit	.01
	Stroke with persistent neurologic deficit	.001
	Transient ischemic attack	.02
Stroke (asymptomatic patients)	Angina (within 30 days prior to operation)	.05
	Functional status (partially dependent)	<.01
	Myocardial infarction (within 6 months prior to operation)	.05
Death (all patients)	Age	<.001
	Chronic obstructive pulmonary disease	<.01
	Disseminated cancer	<.01
	Dyspnea (with moderate exertion)	<.01
	Impaired sensorium[a]	.01
	Myocardial infarction (within 6 months prior to operation)	.05
	Peripheral vascular disease	<.001
Death (symptomatic patients)	Age	<.01
	Disseminated cancer	.02
	Peripheral vascular disease	<.001
	Prior operation within 30 days	<.01
Death (asymptomatic patients)	Age	.001
	Chronic obstructive pulmonary disease	<.001
	Impaired sensorium[a]	<.01
	Myocardial infarction (within 6 months prior to operation)	<.01

[a]Defined as mental status change (confusion and/or delirium) within 48 hours prior to the operation.